Please amend the specification as follows:

Please replace the paragraph bridging pages 12 and 13 with the following paragraph.

Figure 15 shows engineering and expression of immunoglobulin H chain gene with two heterologous epitopes. Panel A shows a schematic representation of mutagenesis vectors, introduction of the (NANP)3 (SEQ ID NO: 39) and NANPNVDPNANP (SEQ ID NO: 9) coding sequences and partial, nucleotide sequence of CDR2 (SEQ ID NO: 10) and CDR3 (SEQ ID NO: 11) after insertion. The synthetic oligonucleotides and the mutagenesis steps for the creation of pVH-TAC/CCA are detailed in the Experimental Protocol. Two pairs of complementary synthetic oligonucleotides coding for (NANP)3 (SEQ ID NO: 39) and NANPNVDPNANP (SEQ ID NO: 9), were cloned in the Asp718 site in CDR3 and in the NcoI site in CDR2 of pVH-TAC/CCA. The insertions were verified by dideoxy- chain-termination sequencing. Panel B shows a schematic representation of plasmid DNA γ1NV^{2}NA^3 carrying the coding sequences for the two heterologous epitopes in CDR3 and CDR2, respectively. The human γ1 constant (C) region gene is in genomic configuration. CHI, CH2, and CH3 refers to the corresponding domains in the C region of the γ1 gene. Promoter (Pr) and enhancer (En) elements for tissue-specific expression and the neomycin (Neo^r) and ampicillin (Amp^r) resistance genes are indicated. Panel C shows a schematic representation of antigenized H chain gene product paired with a light chain. The engineered epitopes in CDR3 and CDR2 are as indicated (not to scale).

Please replace the description of Figure 17 on page 14 with the following paragraph.

Figure 17 shows in vivo immunogenicity of CDR3 and CDR2 epitopes. Mice were immunized with plasmid DNA γ1NANP (black squares) or γ1NV^{2}NA^3 (open squares). Their sera were tested by ELISA on synthetic peptide (NANP)n (SEQ ID NO: 4) (panels A and B) or NANPNVDPNANP (SEQ ID NO: 9) (panels C and D). Values refer to absorbance (492 nm) of sera tested at 1:1600 dilution and are expressed as the

mean (± standard error). Each group consisted of four mice. (*) indicates statistical significance between the values shown in panel B versus panel A. Significance was $p<0.01$ on day 7, and $p<0.05$ on day 14. Time refers to days after DNA inoculation. Please replace the paragraph bridging pages 14 and 15 with the following paragraph.

Figure 19 shows a schematic representation of plasmid DNA γ1NANP, γ1NANP/GM-CSF and γ1NANP / IL-2 . Panel A shows γ1NANP is a variant of γ1WT, the product of the fusion between a human γ1 C region gene present in the plasmid vector pNeoγ1 with murine V_H^{62} gene (2.3 kb) (Sollazzo et al., supra, 1989). In this productively rearranged V_H region gene, the CDR3 was modified to code for three repeats of the Asn-Ala-Asn-Pro (NANP) (SEQ ID NO: 4) sequence (Sollazzo et al., supra, 1990a). The C region gene is in genomic configuration. Panel B shows that, in plasmid DNAγ1NANP /GM-CSF (granulocyte monocyte-colony stimulating factor), the murine GM-CSF coding sequence was cloned at the 3' end of the CH3 domain. Panel C shows that, in plasmid DNA γ1NANP/1L-2, the murine 1L-2 coding sequence was similarly cloned at the 3' end of the CH3 domain. Each plasmid DNA carries the regulatory elements, promoter (Pr) and enhancer (En) needed for 5 tissue-specific expression. Neo^r = neomycin and Amp^r = ampicillin, are the resistance genes.

Please replace the paragraph bridging pages 19 and 20 with the following paragraph.

Figure 33 shows a schematic representation of plasmid DNA γ1NP. This H-chain coding plasmid is the product of the fusion of a human y1C region with a murine V_H engineered to express the 13 amino acid residues from the sequence of the influenza virus nucleoprotein (NP) antigen (366-379) in the third complementarity- determining region (CDR3). This NP peptide is presented in association with the D^b allele in H-2^b mice. The coding strand of the CDR3 region is shown in bold, with the NP-coding sequence underlined (SEQ ID NO: 12). The amino acid sequence of the influenza peptide ^{366}ASNENMETMESSTL$^{37}{}_9$ (SEQ ID NO: 13) is shown in bold. B, BamHI; RI, EcoRI; Neo, neomycin (G418) resistance; Amp, ampicillin resistance. The H-chain gene was mutagenized to introduce a single KpnI/Asp718 site and complementary oligonucleotides

5' GTA CCC GCT TCC AAT GAA AAT ATG GAG ACT ATG GAA TCA AGT ACA CTT 3' (SEQ ID NO: 14) 5' GTA CAA GTG TAC TTG ATT CCA TAG TCT CCA TAT TTT CAT TGG AAG CGG 3' (SEQ ID NO: 42) coding for residues 366-379 of the influenza virus NP antigen (ASNENMETMESSTL) (SEQ ID NO: 13) were introduced between 94V and 95P of the mutagenized V_H region. The engineered V_HNP coded by the 2.3 kb EcoRI fragments was cloned upstream from a human γ1 constant (C) region gene contained in the 12.8 kb vector pNγ1.

Please replace the description of Figure 34, on page 20, with the following paragraph.

Figure 34 shows survival curves in mice vaccinated with plasmid DNA γ1NP (DNA) via intraspleen inoculation and challenged with x10LD_{50} influenza virus. Other groups were primed with plasmid DNA γ1NP followed by a booster with synthetic peptide the influenza virus NP antigen ASNENMETMESSTL (SEQ ID NO: 13) in immunologic adjuvant (DNA + peptide), or NP synthetic peptide ASNENMETMESSTL (SEQ ID NO: 13) in immunologic adjuvant followed by a booster with the same synthetic peptide (peptide + peptide). Challenge with the virus was given three months after priming.

Please replace the paragraph bridging pages 20 and 21 with the following paragraph.

Figure 35 exemplifies the engineering of an immunoglobulin H chain gene with two heterologous Th cell epitopes. The H chain gene is coded by plasmid vector γ1NV2VTSA3. The V_H region is the 2.3 kb Eco RI genomic fragment containing the VDJ rearrangement of a murine V region gene (see Figure 1 for detail). The human γ1 constant (C) region gene is in genomic configuration. CHI, CH2, and CH3 refers to the corresponding domains in the C region of the γ1 gene. Promoter (Pr) and enhancer (En) elements for tissue-specific expression and the neomycin (Neo^r) and ampicillin (Amp^r) resistance genes are indicated. The V_H region is modified by mutagenesis to code for two heterologous determinants as indicated in the right panel. The arrow points the structure of the translated protein composed of the transgenic H chain and a light (L) chain provided by the host cell. The amino acid sequences in the CDR2 and CDR3, are

indicated and correspond to the Th cell determinant NANPNVDPNANP (SEQ ID NO: 9) from the outer coat of the malaria parasite *P. falciparum* (in CDR2) and the VTSAPDTRPAP (SEQ ID NO: 15) epitope from the tandem repeat of the tumor antigen MUC- 1 (in CDR3). CDR= complementarity determining region. H = heavy (chain); C = constant region. Not to scale.

On page 21, please replace the description of Figure 36 with the following paragraph.

Figure 36 shows the effect of linked recognition of a dominant Th epitope and a cryptic/subdominant Th epitope on the proliferative response to the cryptic/ subdominant epi tope. Th/Th associative recognition is necessary to render immunogenic T cell determinant from the MUC-l antigen. Mice were inoculated with plasmid DNA as indicated. Spleen cells were harvested on day 15 and re-stimulated *in vitro* for 4 days in the presence of 50 μg /ml of synthetic peptide (DTRP)3 (SEQ ID NO: 16) and VTSAPDTRPAP (SEQ ID NO: 15) (denoted as VTSA) . Both sequences are contained in the PDTRPAPGSTAP (SEQ ID NO: 17) tandem repeat of the tumor antigen MUC-l. Superscript numbers indicate the CDR in which the heterologous antigen sequence has been inserted. Subscript numbers indicate the number of times the sequence in brackets is repeated in the context of a particular CDR. The results shown are cumulative of three independent experiments. Each group is constituted of 8-10 mice. Results are expressed as stimulation index. Bars indicate means of stimulation indexes ± SEM.

Please replace the paragraph bridging pages 47 and 48 with the following paragraph.

As disclosed herein in Example III, immunity against the human malaria parasite *Plasmodium falciparum* was induced using somatic transgene immunization, a method to effectively target B lymphocytes *in vivo*. A single inoculation of plasmid DNA containing an immunoglobulin heavy chain gene coding in the CDR3 for three repeats of, the sequence Asn-Ala-Asn-Pro (NANP) (SEQ ID NO: 4), a B-cell epitope of *P. falciparum* sporozoites, induced antibodies against NANP (SEQ ID NO: 4) in all mice. Immunologic memory was also established as revealed by booster with an antibody

antigenized with the NANP (SEQ ID NO: 4) peptide administered in adjuvant or through challenge with *P. falciparum* sporozoites. During the primary response, anti-NANP antibodies were primarily IgM and IgG2a. After booster, all antibody isotypes, including IgG1, developed readily. Thus, immunity to a parasite antigen can be induced by exploiting mechanisms in which B lymphocytes are both the source of the immunogen as well as the effector mechanism of immunity. The results disclosed herein indicate that somatic transgene immunization is an effective approach for vaccination against foreign pathogens.

Please replace the paragraph bridging pages 67 and 68 with the following paragraph.

For extraction of genomic DNA from spleen tissue and genomic DNA sequencing, spleens were harvested 17 days after DNA inoculation, frozen at -170°C and the cells were prepared by tissue grinding in liquid nitrogen. Typically the genomic DNA was extracted from 10 mg of spleen tissue using the QIAamp Tissue Kit (Qiagen Inc.; Chatsworth CA). Two specific primers, TTATTGAGAATAGAGGACATCTG (SEQ ID NO: 22) and ATGCTCAGAAAACTCCATAAC (SEQ ID NO: 23) for the murine V_H^{62} were used to amplify by PCR a segment of 520 bp from genomic DNA. The PCR conditions were as follows: 45 sec at 94°C, 45 sec at 54°C and 45 sec at 72°C for 30 times. The PCR products were cloned in pGEM-T vector (Promega; Madison WI). Six clones from the genomic DNA of the spleen inoculated 17 days earlier and four clones from the genomic DNA of tranfectoma B cells (Sollazzo et al., supra, 1989) were sequenced on both strands by dideoxy termination method with Sequenase 2.0 DNA sequencing kit (USB; Cleveland OH) using two primers, AACAGTATTCTTTCTTTGCAGG (SEQ ID NO: 24) and TTATTGAGAATAGAGGACATCTG (SEQ ID NO: 22), annealing 10 bp before the first codon of the FR1 and at the 3' end of the FR4, respectively.

Please replace the paragraph bridging pages 76 and 77 with the following paragraph.

Ten milligrams of the tissue were digested in the presence of protease and the cell lysates were loaded onto the QIAamp spin column (Qiagen, Inc.; Chatsworth CA). After

washing twice by centrifugation, the DNA was eluted from the column with distilled water and quantitated on a 1% agarose gel. PCR was performed with a total of four sets of primers, pCL and pCD; pSE and pNAD; pNEL and pNED; and pγA1 and pγA2. pCL (from -107nt to -85nt: 5'-TTATTGAGAATAGAGGACATCTG-3'; (SEQ ID NO: 22) and pCD (from 459nt to 439nt: 5'-ATGCTCATAAAACTCCATAAC-3' (SEQ ID NO: 25); were used to amplify the whole VDJ region of the transgene. pSE (from -32nt to -11nt: 5' -AACAGTATTCTTTCTTTGCAGC-3' (SEQ ID NO: 26); and pNAD (from 352nt to 333nt: 5' -GAGAGTAGGGTACTGGGTTT-3' (SEQ ID NO: 27); were specific for amplification of the genetic marker, $(NANP)_3$ (SEQ ID NO: 39) in CDR3. pNEL (from 169nt to 189nt: 5'- AGCACCTACTATCCAGACACT-3' (SEQ ID NO: 28); and pNED (from 366nt to 346nt: 5' -GTAGTCCATACCATGAGAGTA-3' (SEQ ID NO: 29); were the inner primers for nested PCR. pγAl (from 184nt to 201nt: 5'-TGGGCCGCCCTAGTCACC-3' (SEQ ID NO: 30); and pγA2 (from 427nt to 408nt: 5'-CGTTTGGCCTTAGGGTTCAG-3' (SEQ ID NO: 31); were designed to amplify the murine ß-actin gene according to the sequence indicated in (Harris et al., Gene 112:265-266 (1992)). The PCR consisted of 30 cycles at 94°C for 45 sec, 58°C for 45 sec, and 72°C for 45 sec; 0.3 μM each primer; 0.2 mM each deoxynucleotide; 1.5 mM $MgCl_2$ in 20 mM Tris-HCl, pH 8.4 and 50 mM KC1; and 1 unit of *Taq* DNA polymerase (Gibco BRL; Gaithersburg MD). PCR products for Southern blot analysis were resolved in 1% w/v agarose gel and blotted onto HYBOND-N nylon membrane (Amersham; Cleveland, OH). The membranes were hybridized with the oligonucleotide pNAD labeled using T4 polynucleotide kinase forward reaction in presence of (γ^{32}P-ATP).

Please replace the paragraph bridging pages 92 and 93 with the following paragraph.

Plasmid γ1NV^2NA^3 was engineered as described below. The EcoRI fragment of the productively rearranged murine VH (2.3 Kb) was cloned in vector pBluescript II KS to yield plasmid pVH. Site-directed mutagenesis was performed using two 21mer oligonucleotide primers, one (5' -CAAGAAAGGTACCCTACTCTC-3') (SEQ ID NO: 33) annealing in CDR3 to introduce 3bp (TAC, in bold) for the creation of an Asp718 site, and another (5' -AGTAATGGCCATGGTAGCACC-3') (SEQ ID NO: 34) annealing in

CDR2 to introduce 3bp (CCA, in bold) for the creation of a NcoI site. These primers were annealed to the uracylated, complementary strand of pVH and the mutant strands were synthsized and ligated in the presence of T4 DNA polymerase and ligase. Plasmid pVH-TAC/CCA, containing two unique sites, one in CDR3 (Asp718) and the other in CDR2 (NcoI), was obtained after transformation, screening of individual colonies and confirmation by DNA sequencing (SEQUENASE 2.0 DNA Sequencing Kit; USB; Cleveland OH). A pair of complementary oligonucleotides, 5'-GTACCCAATGCAAACCCAAATGCAAACCCAAATGCAAACCCA-3' (SEQ ID NO: 35) (sense) and 5' -GTACTGGGTTTGCATTTGGGTTTGCATTTGGGTTTGCATTGG-3 ' (SEQ ID NO: 36) (antisense) coding for the (NANP) 3 sequence (SEQ ID NO: 39) was synthesized, annealed and cloned in the Asp718 site. A pair of complementary oligonucleotides 5'-CATGGTAATGCAAACCCAAATGTAGATCCCAATGCCAACCCA-3' (SEQ ID NO: 37) (sense) and 5' -CATGTGGGTTGGCATTGGGATCTACATTTGGGTTTGCATTAC-3' (SEQ ID NO: 38) (antisense) coding for the NANPNVDPNANP (SEQ ID NO: 9) sequence was similarly cloned into the NcoI site. The insertions and the proper orientation were verified by dideoxy sequencing (SEQUENASE 2.0 DNA Sequencing Kit; USB) The 2.3Kb EcoRI fragment carrying the engineered CDR3 and CDR2 was then subcloned in the expression vector pNγ1 (Sollazzo et al., *supra*, 1989) upstream from the human γ1constant (C) region using the unique EcoRI site to yield plasmid γ1NV^{2}NA^3. Plasmid γ1NANP carries a productively-rearranged murine V region gene in which only the CDR3 was modified by introducing the nucleotide sequence coding for three NANP (SEQ ID NO: 4) repeats (Sollazzo et al., supra, 1990a). The promoter and enhancer elements in these plasmids are those constitutively existing in Ig H chain genes (Sollazzo et al., *supra*, 1989).

Please replace the paragraph bridging pages 93 and 94 with the following paragraph.

The recombinant antibodies γ1WT and γ1NANP were produced and purified as described previously (Billetta and Zanetti, *supra*, 1992; Sollazzo et al., *supra*, 1989) and

stored at -20°C until use. The synthetic peptide containing multiple repeats of the NANP sequence (SEQ ID NO: 4) was the kind gift of Dr. A. Verdini (Monterotondo, Italy) and peptide NANPNVDPNANP (SEQ ID NO: 9) was ~~synthized~~ synthesized in the peptide synthesis facility of the University of California, Diego.

Please replace the first full paragraph (lines 6-20) on page 94 with the following paragraph.

Antibodies to the (NANP) 3 (SEQ ID NO: 39) and NANPNVDPNANP (SEQ ID NO: 9) peptides were detected by ELISA on 96-well polyvinyl microtiter plate (Dynatech, Gentilly, VA) coated with synthetic peptide (2.5 µg/ml) in 0.1 M carbonate buffer, pH 8.6, by incubation overnight at 4° C. After coating, wells were blocked with 1% BSA in PBS and then incubated overnight at 4°C with mice sera diluted in phosphate buffered saline (PBS), 0.15 M, pH 7.3, containing in 1% bovine serum albumin (BSA) and 0.05 % TWEEN-20. The bound antibodies were revealed using a HP-conjugated goat antibody to mouse Ig absorbed with human Ig (Sigma) (1:10,000 dilution). The bound peroxidase was revealed by adding o-phenylenediamine dihydrochloride and H_20_2. Plates were read after 30 min in a micro-plate reader VMAX; Molecular Devices) at 492 nm.

Please replace the second full paragraph on page 95 with the following paragraph.

The engineering of two distinct epitopes in the same Ig V region gene was performed in the CDR3 and the CDR2 which contain a Asp718 (Sollazzo et al., *supra*, 1990b) and NcoI site , respectively. In the expressed proteins, both CDRs are loops interconnecting ß-strands on the same ß-sheet of the V domain. A modification of these two CDRs was expected to be compatible with proper VH/VL scaffolding, whereas engineering of the CDR1, which connects two different sheets of the V domain, could result in misfolding of the polypeptide. The B cell epitope used consisted of three repeats of the tetrapeptide Asn-Ala-Asn-Pro (NANP) (SEQ ID NO: 4) from the CS antigen of *P. falciparum* parasite (Zavala et al., supra, 1985).

Please replace the paragraph bridging pages 95 and 96 with the following paragraph.

The Th cell epitope used is the peptide Asn-Ala-Asn-Pro-Asn-Val-Asp-Pro-Asn-Ala-Asn-Pro (NANPNVDPNANP) (SEQ ID NO: 9), a conserved peptide sequence located in the 5' region of the CS antigen of *P. falciparum*. This peptide is recognized by immune human $CD4^+$ T lymphocytes (Nardin, et al., Science 246: 1603-1606 (1989), is immunogenic for several MHC haplotypes in the mouse (Munesinghe et al., *supra*, 1991) and has been included in multiple-antigen-peptide vaccines for malaria.

Please replace the first full paragraph on page 96 with the following paragraph.

The CDR3 and CDR2 of pVH were engineered as illustrated in Figure 15. The 2.3 Kb EcoRl DNA fragment carrying a productively-rearranged murine V_H cloned into pBluescript (pVH) was modified by oligonucleotide site-directed mutagenesis to introduce two unique cloning sites, Asp 718 site in CDR3 (Sollazzo et al., *supra*, 1990a) and Ncol in CDR2 (pVH-TAC/CCA). A pair of complementary synthetic oligonucleotides coding for three NANP (SEQ ID NO: 4) repeats was cloned into the Asp 718 site whereas the pair coding for the NANPNVDPNANP sequence (SEQ ID NO: 9) was cloned into the Ncol site of pVH-TAC/CCA. Nucleotide insertion and the correct orientation were checked by PCR and confirmed by sequencing (Figure 15A). The engineered 2.3 Kb EcoRl fragment was then cloned into the unique EcoRl site of the expression vector pNγ1 to yield plasmid $\gamma 1NV^2NA^3$ (Figure 158). The V region gene of plasmid $\gamma 1NV^2NA^3$ codes, therefore, for two distinct epitopes of the CS antigen, one in CDR3 and the other in CDR2.

Please replace the first full paragraph on page 97 with the following paragraph.

To determine *in vivo* immunogenicity, immunogenicity of secreted transgene H chain Ig carrying the two heterologous epitopes was analyzed by direct intraspleen inoculation of plasmid $\gamma 1NV^2NA^3$ and by comparing the antibody response in these mice

to that of mice inoculated with plasmid γ1NANP. All mice mounted a humoral antibody response to the human constant region of the transgene product proving that immunization took place. Mice of both groups produced anti- (NANP) 3 antibodies, indicating that in both instances, the CDR3 loops were immunogenic (Figure 17). However, the anti- NANP response in mice inoculated with plasmid $\gamma 1NV^2NA^3$ was higher than in mice inoculated with plasmid γ1NANP (Figure 17A versus 17B). Interestingly, whereas mice inoculated with plasmid $\gamma 1NV^2NA^3$ produced antibodies reactive against both (NANP) 3 (SEQ ID NO: 39) and NANPNVDPNANP (SEQ ID NO: 9) peptides (Figure 17B and 17D), mice inoculated with plasmid γ1NANP produced antibodies against (NANP) 3 (SEQ ID NO: 39) only (Figure 17A and 17C). Because antibodies to (NANP) 3 (SEQ ID NO: 39) do not cross-react with NANPNVDPNANP (SEQ ID NO: 9), mice inoculated with plasmid $\gamma 1NV^2NA^3$ produced two distinct populations of antibodies, one against the (NANP) 3 peptide (SEQ ID NO: 39) in CDR3 and the other against the NANPNVDPNANP peptide (SEQ ID NO: 9) in CDR2.

Please replace the second full paragraph on page 112 with the following paragraph.

After animals were inoculated, at the time of harvest, mice were sacrificed and the lymph nodes and spleens removed, and crushed in a tissue shredder to remove excess tissues and release cells. Single cell suspensions were treated with red blood cell lysis buffer (Sigma; St. Louis, MO) and cultured (10^6 cells/ml) in RPMI 1640 medium (Irvine Scientific; Santa Ana CA) supplemented with Hepes buffer, glutamine, 7.5% fetal calf serum and 50 μM 2-mercaptoethanol, in the presence or absence of synthetic peptides NANPNVDPNANP (SEQ ID NO: 9) or NANPNANPNANP (SEQ ID NO: 39)(50 μg /ml) in triplicate. The cells were incubated at 37°C in 10% CO_2 for 3 days (^3H) Thymidine was added at 1μCi/well and the cells were incubated for 16-18 hours at 37°C. Cells were harvested onto glass fiber filter mats using a Tomtec cell harvester and the radioactivity was measured in a liquid scintillation counter (Betaplate; Wallac; Tuku Finland). Results are expressed as Stimulation Index (S. I.) calculated as the ratio of (counts per minute of cells cultured in the presence of synthetic peptide) / (counts per

minute of cells cultured in the absence of peptide). Concanavalin A (ConA) stimulation was used as a polyclonal activator and positive control.

Please replace the paragraph bridging pages 114 and 115 with the following paragraph.

The effects of STI on activation of T lymphocytes was determined. T cell responses were assessed using DNA coding for 12 amino acid determinants of the circumsporozoite (CS) protein of *Plasmodium falciparum* malaria parasite. The plasmid $\gamma 1NV^2NA^3$ DNA contains an Ig H chain gene in which the V domain is engineered to code for a Th cell determinant (NANPNVDPNANP) (SEQ ID NO: 9) in CDR2 and a B cell epitope (NANPNANPNANP) (SEQ ID NO: 39) in CDR3 (antigenized antibody) The Th cell determinant (-NVDP-) (SEQ ID NO: 40) and the B cell epitope only differ by two amino acid residues, A to V and N to D in position 5 and 6, respectively. As disclosed in Example IV, an antigenized antibody product of the same gene, when injected in complete Freunds' adjuvant, induces specific T cell proliferation and IL-2 secretion.

Please replace the first full paragraph on page 115 with the following paragraph.

Spleen cells harvested 7 days after a single intraspleen inoculation of 100 μg of $\gamma 1NV^2NA^3$ DNA proliferated in culture after re-stimulation with the antigenized antibody expressing the Th cell determinant or the corresponding 12mer Th cell determinant peptide (Figure 27A). Proliferation occurred when cells were cultured with the T- but not the B-cell peptide demonstrating specific activation by the heterologous peptide in CDR2. Proliferation after culture with the antigenized antibody expressing -NVDP- (SEQ ID NO: 40) also suggests that the CDR2 peptide within the antibody molecule is processed and presented by APC. When compared with the proliferative response of cells from mice immunized with the antigenized antibody in CFA, STI induced a response of similar or greater magnitude. Specific activation of T cells was accompanied by marked production of IL-2 (Figure 27B). The lower amounts of IL-2 measured in cultures re-stimulated *in vitro* with the -NVDP- (SEQ ID NO: 40) peptide most likely reflect a higher consumption as cells in these cultures were proliferating to a greater extent.

Please replace the paragraph bridging pages 124 and 125 with the following paragraph.

Early studies *in vitro* demonstrated that a B cell harboring an If H chain transgene process and present in a T cell peptide to cytotoxic (CD8) T cells, and are lysed with high efficiency (Billetta et al., Eur. J. Immunol. 25:776-783 (1995)). For instance, when B-lymphoma cells (Db) were transfected with the H chain gene engineered to express in the third DCR the NP peptide ASNENNETMESSTL (SEQ ID NO: 13) they were efficiently killed by specific CTL in a dose-dependent manner indicating that. processing the presentation of the NP peptide at the surface of the cell had occurred. Killing was MHC-restricted and blocked by an anti-class-I MHC monoclonal antibody.

Please replace the second full paragraph on page 126 with the following paragraph.

Two H-chain genes were engineered to express in the CDR3 two amino acid sequences (VTSAPDTRPAP (SEQ ID NO: 15)and DTRP3 (SEQ ID NO: 16)) from the tandem repeat of the tumor antigen MUC-1 (Gendler et al., Proc Natl Adad Sci USA, 84: 6060- 6064 (1987)). Each gene coding for a single epitope of the MUC-1 antigen was also engineered to code in the CDR2 for the Th cell determinant NANPNVDPNANP (SEQ ID NO: 9) from the outer coat of the malaria parasite *P. Falciparum* (Nardin et al., Science 246:1603-1606 (1989)). The corresponding plasmid vector is termed y1NV2VTSA3 (Figure 35) and y1NV2DTRP3.